

REMARKS

In the Office Action dated May 27, 2003, claim 16 was rejected under 35 U.S.C. § 112, claims 1, 2, 6 and 7 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Nutter *et al.* (WO 98/11883) in view of Todd *et al.* (U.S. Patent 5,082,975), and claims 3-5, 12-21 and 23-25 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Nutter *et al.* in view of Todd *et al.* and Lefren *et al.* (U.S. Patent No. 4,431,427). Claims 8 and 22 were objected to as being dependent upon a rejected claim but would be allowable if rewritten.

Claim Amendments

Claim 2 has been incorporated into claim 1. Claim 13 has been incorporated into claim 12. Claim 16 has been incorporated into claim 15. Claim 24 has been incorporated into claim 23. Claims 2, 13, 16 and 24 have been cancelled accordingly.

35 U.S.C. § 112

The cancellation of claim 16 removes the 35 U.S.C. § 112 rejection.

35 U.S.C. § 103(a)

Independent claims 1, 12, 15 and 23 now recite the concentration of the compound selected from the group consisting of hexahydro beta acids, hexahydro beta salts, tetrahydroiso alpha acids, and tetrahydroiso alpha salts. Specifically, the compound is recited as being in the range of from about 0.2 ppm to about 25 ppm. This limitation was in previous claims 2, 13, 16 and 24. It is believed that this limitation distinguishes amended independent claims 1, 12, 15 and 23 from the prior art.

In particular, the Office Action suggests that Todd *et al.* (U.S. Patent 5,082,975) teaches that the administration of hexahydrocolupulone (HHC) at a concentration of

between 0.2 and 25 ppm will lessen the inhibition of lactobacilli, thus allowing lactobacillus to grow. However, this assertion is not supported by Todd *et al.* as the reference does not state anywhere that HHC concentration levels below 50 ppm will lessen the inhibitory effect of HHC on lactobacilli, and hindsight created by the present application should not be used to support such a conclusion. The Todd *et al.* reference should be reviewed for what it teaches, and it teaches only that lactobacillus may be killed at concentration levels above 50 ppm.

The Office Action infers from the fact that Todd *et al.* describes the use of HHC at concentrations greater than 50 ppm that concentrations below 50 ppm would not inhibit the growth of lactobacilli. However, this inference is neither supported by Todd *et al.* nor by any other evidence provided by the Office Action. Instead, the Office Action relies upon an argument of logic and the present application. The problem is that Todd *et al.* does not report any experiments being conducted at concentrations below 50 ppm and therefore provides no guidance whatsoever as to whether and at what concentrations below 50 ppm HHC will stop inhibiting lactobacilli growth and proliferation. In the absence of any evidence to the contrary, one of ordinary skill in the art could readily believe that concentrations as low as 0.2 ppm could also be effective in preventing the growth of lactobacillus.

In this regard, attention is directed to the far right hand column of Table 1 of the present application. When testing hexahydro beta acid at concentrations of 50 and 100 ppm for *Staphylococcus aureus* inhibition, no growth of *Staphylococcus aureus* was observed. Also, at concentrations of 0.2 to 25 ppm, no growth of *Staphylococcus aureus* was observed. Thus, the activity at 50 and 100 ppm in no way provided a

prediction of the activity at 0.2 to 25 ppm. In other words, lowering the concentration did not automatically lessen the inhibitory action. Therefore, it cannot be flatly stated that lower concentration equals lower inhibitory action. It is believed that this data fulfills the request at the top of page 5 of the Office Action for scientific data regarding inhibitory action at lower concentration levels.

The data for *Staphylococcus aureus* inhibition by hexahydro beta acids demonstrate the unpredictability of antibacterial action. It quite simply cannot be predicted that lower concentrations will lessen inhibitory action. As a result, Todd *et al.* should not be offered for the premise that it would have been obvious to one of ordinary skill in the art to employ HHC concentration levels below 50 ppm, and more particular in the range of 0.2-25 ppm, to lessen the inhibitory effect of HHC on lactobacilli. The above data indicate that the activity of HHC at lower concentrations is unpredictable. Thus, one skilled in the art would not automatically conclude that lowering the concentration level would lower inhibitory activity. For this reason, the Applicants respectfully submit that the amended claims are in no way obvious over Todd *et al.*, Nutter *et al.* or Lefren *et al.* taken alone or in combination.

In order to provide further evidence of the unpredictability of antibacterial action, there is attached a Declaration of the first named inventor. The inventor's Declaration makes it clear that without the benefit of the experiments reported in the above-identified patent application, it would have been impossible to predict the effects of a lower concentration of HHC (such as in the range of 0.2-25 ppm) on the growth of lactobacilli. It is further noted that even though Todd *et al.* show that hexahydrocolupulone inhibits the growth of certain lactobacilli in milk (pH 6.4-6.8) at 50-

200 ppm, these experiments cannot be used to predict lactobacilli anti-bacterial action at the vaginal pH of 4.5-5.0. Thus, the activity of hop acids on lactobacilli below the 50 ppm level reported in Todd *et al.* at vaginal pH of 4.5-5.0 could not be predicted from Todd *et al.*

Conclusion

The Applicants respectfully submit that amended claims independent claims 1, 12, 15 and 23 (and claims 3-8, 14, 17-22 and 25 that depend thereon) are in condition for allowance. Favorable reconsideration is respectfully requested.

A fee sheet is attached for the two month extension. No additional fees are believed to be needed for this amendment. However, if additional fees are needed, please charge them to Deposit Account No. 17-0055.

Respectfully submitted,

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